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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/784,553	02/16/2001	Ming-Ming Zhou	2459-1-003 CIP	3124
23565	7590	08/10/2004	EXAMINER LUCAS, ZACHARIAH	
KLAUBER & JACKSON 411 HACKENSACK AVENUE HACKENSACK, NJ 07601			ART UNIT 1648	PAPER NUMBER
DATE MAILED: 08/10/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/784,553	Applicant(s) ZHOU ET AL.	
	Examiner Zachariah Lucas	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 June 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) 1-4 and 9-36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5-8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>7-8-02</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II, subgroup (A), and the species represented by SEQ ID NO: 19 in the reply filed on June 21, 2004 is acknowledged. The traversal is on the ground(s) that all of the sequences falling within the genus described by SEQ ID NO: 3 may be searched without undue burden. This is not found persuasive because each of these sequences requires a separate search. However, the Office agrees with Applicant's assertion that the sequences described by SEQ ID NO: 3 share a common structure. The restriction among these inventions is therefore reformed as a species election, and the election of SEQ ID NO: 19 is treated as an election of species.

The reformed restriction requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-4, and 9-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 21, 2004.

3. Claims 5-8 are pending to the extent that they read on the elected subject matter.

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Sequence Listing

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below. The specification discloses SEQ ID NO: 3 on page 18 of the application. The newly submitted paper copy of the sequence listing does not match the sequence identified on page 18. This is because the residue noted as J_{Y/F/H} in the sequence (indicated on page 19 to indicate that the residue may be a tyrosine, phenylalanine, or a histidine), does not appear to be properly included in the paper copy of the sequence listing. In particular, this residue appears to correspond to residue 16 of the SEQ ID NO: 3 in the paper listing, which the paper listing indicates may be any of a Proline, Lysine, or a Histidine. Thus, the paper listing does not match the sequences provided in the specification as filed.

Applicant is given the response period of the present action within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. Direct the reply to the undersigned.

Information Disclosure Statement

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5. The information disclosure statement (IDS) submitted on July 8, 2002, is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 5-8 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. These claims read on peptides comprising a bromodomain according to SEQ ID NO: 3 (disclosed on page 18 of the application). While the specification indicates that a peptide “can be” a fragment of a bromodomain (page 25), and that a peptide is “preferably...a compound of at least two but less than fifty subunit amino acids,” the specification does not provide any specific structural limit the definition of a peptide according to the claimed invention. Further, the definition of a peptide in the art requires only that the peptide comprise two or more amino acids. See e.g., Stedman's Online Medical Dictionary, 27th Edition (definition for “peptide”). Thus, the claims include embodiments wherein the claimed peptide is a naturally occurring protein comprising a bromodomain. It is suggested that the claims be amended to read on an isolated peptide.

8. Claims 5-8 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. These claims broadly read on any peptides comprising a sequence according to the generic formula of SEQ ID NO: 3, or on peptides comprising SEQ ID NO: 19. The

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specification asserts no utility for these peptides other than that they may be used to identify ligands and modulators of bromodomain binding. The asserted utility is rejected because the claims do not appear to meet the “specific and substantial” utility criteria for the claimed peptides in general. The claims are rejected for two reasons. First, with respect to claims 5 and 6, there is no requirement that the peptides contain sequences from naturally occurring proteins. However, because the utility of the peptides is based on their ability to bind ligand proteins and to identify modulators of such binding between the bromodomain and the ligand protein, and because there would be no natural ligand to non-naturally occurring ZA loops, there no utility asserted for such non-naturally occurring peptides.

Second, with respect to claims 5-8, the application does not provide a specific and substantial utility for the peptide of SEQ ID NO: 19. The Applicant has neither identified the binding partner of the bromodomain comprising peptide, nor identified a disease or disorder associated with the interaction between the two molecules. While the application indicates that the peptides may be useful for the identification of pharmaceuticals, absent a suggestion as to what disorders or diseases may be treated with the peptide or the modulators of its binding, the asserted utility is not adequately specific to meet the utility requirement. See MPEP § 2107.01 (stating indicating that a compound may be useful in treating unspecified disorders, or that the compound has “useful biological” properties, would not be sufficient to define a specific utility for the compound,” but stating that “where an applicant discloses a specific biological activity and reasonably correlates that activity to a disease condition” a specific utility has been asserted.” In the present case, because there is no assertion of a specific utility for the claimed peptides, the claims are rejected under 35 U.S.C. § 101.

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Claims 5-8 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claim describe a genus of inventions comprising peptides comprising the ZA loop of a bromodomains, wherein the bromodomains have between 21-40 amino acids. However, the specification teaches that bromodomains have about 110 amino acids. See e.g., page 3, lines 1-2. These teachings are supported by those of Jeanmougin et al. (TIBS 22:151-53, page 151- of record in the IDS of July 2002). In addition to teaching that bromodomains have over 100, rather than 21-40 amino acids, the application also fails to provide any examples of bromodomains of between 21-40 amino acids. The application therefore does not provide written

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description support for claims drawn to peptides comprising a bromodomain of 21 to 40 amino acids because the Applicant has not provided any evidence that such bromodomains exist.

However, it is noted that the specification also indicates that there is a 21-40 amino acid region within bromodomains referred to as the ZA loop. It is thus suggested that the claims be amended to read on peptides wherein the ZA loop has between 21 to 40 amino acids.

11. Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims read on peptides comprising the ZA loop of protein bromodomains that fall within an indicated generic structure, that of SEQ ID NO: 3.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

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The claims describe the genus of peptides as indicated above. The specification indicates that the peptides are useful for the identification of binding partners for proteins comprising acetyl-lysines, and for the identification of compounds useful for the modulation of bromodomain/acetyl-lysine interactions. However, the application does not provide any other uses for the peptides other than in methods for such identification. Nor does the application indicate what the compounds identified in such methods would be useful for. While the application suggests, on pages 20-22, that modulators of certain bromodomain/ligand binding may be useful for the treatment of certain disorders, there is no demonstration that such would be the case with every bromodomain/ligand modulating agent. In addition, while the application provides suggestions as to the potential uses of two bromodomain binding modulators, there is little guidance as to either the ligands, or use of ligand binding modulators, for the claimed peptides in general.

In addition to the limited guidance provided by the application, the art indicates that proteins comprising bromodomains perform a wide number of functions, the scope of which are not presently known, and bind a wide range of other conserved domains. See e.g., Jeanmougin, page 153. Further, the specification itself indicates that the range of binding partners for any particular bromodomain is unknown. See e.g., page 3, lines 13-15. Thus, the claims read on peptides, the only use asserted for which is the identification of ligands to the peptides and of modulators to the binding of the peptides to such ligands. However, the art indicates that the functions and the binding partners of the peptides are generally not known. Thus, in view of the teachings indicated above, those in the art not know how, or for what purpose, to use either the peptides, or the compounds identified using them.

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Because the application provides neither examples nor guidance as to the use of the peptides (or the compounds identified using them), and because those in the art would not be able to use such compounds without both identifying the ligands and modulators, and determining what the functions of the identified compounds are, and in view of the breadth of the claims (drawn to any peptide comprising a ZA loop according to SEQ ID NO: 1), the application does not provides sufficient information to enable those in the art to use the claimed peptides without undue experimentation.

Further, the claimed peptides require the presence only of the ZA loop of a bromodomain. However, the art indicates that such may be not be sufficient to identify either the binding partner to the protein, or modulators thereof. For example, Zeng et al. (FEBS Letters 513: 124-28, at 126) states that the binding domain of the P/CAF “is indeed localized to the hydrophobic cavity between the ZA and BC loops.” While the reference provides teachings indicating that the sequence of the ZA loop is important to the binding and binding specificity of bromodomains (pages 126-27), the statement above indicates that other regions within the binding domain may also be required for ligand binding. In addition, it is noted that there are no examples in the application of peptides comprising only the ZA loop of a bromodomain binding to an appropriate ligand. In view of the teachings that other regions of the protein than the ZA loop may be required for ligand binding, because the Applicant has not provided examples of peptides comprising only ZA loops that bind to ligands, and because the uses provided by the application for the claimed peptides required the ability of the peptides to bind to ligands, the Applicant is not enabled for the claimed peptides comprising only the ZA loops of the bromodomains.

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Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

13. Claims 5 and 6 are rejected under 35 U.S.C. 102(a) as being anticipated by Dhalluin et al. (Nature 399:491-96- of record in the July 2002 IDS). These claims read on peptides that comprise a ZA loop of a bromodomain comprising SEQ ID NO: 3, and fusion proteins thereto. Dhalluin teaches a bromodomain comprising a ZA loop according to SEQ ID NO: 3. See, Figure 1 (esp. the peptide of residues 719-832 of the hsP/CAF bromodomain). Further, the reference teaches the making and purification of a fusion protein comprising this sequence and a histidine tail. Page 495, section entitled “Sample Preparation”). The reference therefore anticipates the indicated claims.

Conclusion

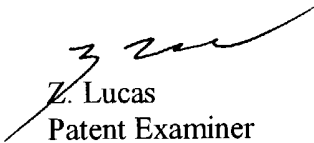
14. No claims are allowed.

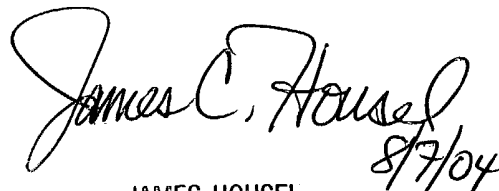
15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Z. Lucas
Patent Examiner


JAMES HOUSEL
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8/7/04